Structural and hemodynamic comparison of anatomical and synthetic cerebral capillary networks

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A computational method is presented for generating synthetic, random 3D capillary networks which match the topological, geometrical and functional properties of the cerebral microcirculation. These networks, which can be generated in volumes larger than can currently be extracted by high-resolution imaging, can then be coupled to lower-resolution data sets of whole-brain vasculature to model blood flow and mass transport, and to validate equivalent continuum/hybrid models. Another motivation is to reveal the dominant structural features of cerebral capillary networks, which can then be tuned to model different brain regions or pathological states such as Alzheimer's disease. Previous works [1, 2] lacked physiological basis, and although resulting networks conformed to expected global morphometric properties, were not subjected to thorough topological or functional analysis.

In contrast, our approach is based on the physiological assumption that the maximum separation of tissue cells from the nearest capillary is limited by the diffusion distance of oxygen [3]. Previously, synthetic, space-filling 2D networks were constructed by placing one point randomly in each cell of an n $\times$ n grid; from this set of points, Voronoi diagrams were extracted with the edges producing a 2D network with mainly three capillaries per vertex, a characteristic feature of cerebral capillary networks. Here, we extend this approach to 3D.

In 3D, Voronoi diagrams produce polyhedrons with many capillaries per vertex. To derive a network with only bifurcations, clusters of vertices were systematically merged and capillaries then removed randomly. Geometrical metrics such as the mean/S.D. of lengths and edge/length/vertex densities were compared to those of capillary regions extracted from mouse cerebral anatomical data sets [5, 6]. Capillary loops were studied to measure the interconnected network topology, while the distribution of extravascular distances allowed comparison of the spatial arrangement of capillaries. Finally, hemodynamic properties were captured through the network permeability. Overall, synthetic networks showed excellent agreement with the anatomical data.

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